Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 10, 11, 16, 17, 18 and 19 are pending in the application, with claims 10 and 11 being the independent claims. Claims 1-9 and 12-15 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Claims 10 and 11 are sought to be amended. Support for the amendment to claim 10 can be found, *inter alia*, in Fig. 3 and support for the amendment to claim 11 can be found, *inter alia*, in Fig. 5 and Example 2 of the specification. New claims 16, 17, 18 and 19 are sought to be added. Support for new claim 16 is found, *inter alia*, at page 2, lines 6-10 and lines 17-22, page 4, lines 17-24, page 6, lines 8-18 and Example 1 of the English language translation of the specification. Support for new claims 17 and 18 is found, *inter alia*, at page 8, lines 23-26 of the English language translation of the specification. Support for new claim 19 is found, *inter alia*, in Table 1, page 10, lines 21-25 and page 12, line 24 through page 13, line 12 of the English language translation of the specification. Support for the amendments to the specification may be found in original claims 12 and 13. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Objections to the Claims

The Examiner has objected to claims 10-12, stating that the mere recitation of "a patient" does not make clear the previous occurrence of hepatocellular carcinoma. Claim 12 has been cancelled, thus this objection is moot with regard to claim 12. The Examiner has suggested inserting the phrase "who has suffered from said carcinoma" after the term "patient" in claim 11, and the phrase "in need thereof" after the term "patient" in claim 10. Applicants submit that the currently amended claims 10 and 11 address the Examiner's objections, and Applicants respectfully request withdrawal of these claim objections.

Rejections under 35 U.S.C. § 101

The Examiner has rejected claims 13 and 14 under 35 U.S.C. §101, alleging that the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process. This rejection is moot in view of the cancellation of claims 13 and 14.

Rejections under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1-5, 10 and 15 under 35 U.S.C. §112, first paragraph, alleging that the specification, while being enabling for treating a hepatic disease or inhibiting the occurrence of portal venous invasion, does not reasonably provide enablement for preventing a hepatic disease or portal invasion. The Examiner has stated that the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing a hepatic disease or portal venous

invasion, or how a patient could be kept from being susceptible to these conditions. The Examiner has further stated that there is no guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for preventing a hepatic disease or portal venous invasion. The Examiner has also stated that the term "prevention" or "preventing" is synonymous with the term "curing" and that both circumscribe circumstances of absolute success. The Examiner alleges that since absolute success is not reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations as complex and poorly understood as a hepatic disease or portal venous invasion, the specification, which lacks a showing that any hepatic disease or portal venous invasion is actually prevented, is viewed as lacking an adequate written description of the same. Applicants note and thank the Examiner for the suggestion to change the term "preventing" to "inhibiting the occurrence of portal venous invasion." Applicants respectfully traverse this rejection.

This rejection is moot in view of cancelled claims 1-5 and 15. With regard to claim 10, Applicants have amended the claim to recite a method of inhibiting the occurrence of portal venous invasion, which the Examiner acknowledged was enabled by the specification. Accordingly, Applicants respectfully request withdrawal of this rejection.

Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 13 and 14 under 35 U.S.C. §112, second paragraph, alleging that the claims are indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner has

stated that these claims provide for the use of menatetrenone for manufacturing an agent and inhibiting recurrence of hepatocellular carcinoma, but do not set forth any steps involved in the method/process. This rejection is moot in view of cancelled claims 13 and 14.

Rejections under 35 U.S.C. § 102

I.

The Examiner has rejected claims 1-9, 13 and 15 under 35 U.S.C. §102(b) as being anticipated by Ida *et al.* (U.S. Patent No. 5,021,570) (hereinafter "Ida *et al.*"). The Examiner has alleged that Ida *et al.* teach a pharmaceutical composition comprising menatetrenone as an active agent as well as a method for manufacturing the composition. In view of the cancelled claims 1-9, 13 and 15, this rejection is moot.

II.

The Examiner has rejected claims 1-9 and 11-15 under 35 U.S.C. §102(b) as being anticipated by Furukawa *et al.* (Furukawa *et al.*, Cancer, Vol. 69, Number 1, pp. 31-38, January 1, 1992) (hereinafter "Furukawa") or under 35 U.S.C. §102(a) as being anticipated by Koike *et al.* (Koike *et al.*, http://ddw02.agora.com/planner/displayabstract.asp?presentationid=31, July 8, 2002) (hereinafter "Koike"). Applicants respectfully traverse this rejection. This rejection is moot with regard to cancelled claims 1-9 and 12-15. Accordingly, the following discussion applies to pending claim 11.

The Examiner has stated that Furukawa teaches that the administration of menaquinone-4 (a.k.a. menatetrenone) to patients suffering from hepatocellular

carcinoma was effective to decrease the patients' plasma level of des-gamma-carboxy prothrombin. The Examiner has further stated that composition of menaquinone-4 containing 50 mg and 10 mg are taught.

The Examiner has stated that Koike teaches that the administration of vitamin K-II (a.k.a. menatetrenone) to patients suffering from hepatocellular carcinoma was effective to inhibit portal venous invasion (PVI). The Examiner has further stated that oral compositions of vitamin K-II (45 mg/day) are also taught.

The Examiner has alleged that with regard to claim 11, Applicants have claimed methods of inhibiting recurrence of hepatocellular carcinoma that require the administration of an effective dose of menatetrenone to a patient. The Examiner has stated that Furukawa and Koike disclose each and every one of the claim limitations except the objective of inhibiting the recurrence of hepatocellular carcinoma. The Examiner has alleged, however, that because the references teach that the same active ingredient is administered to the same patient and in effective amounts as in the present claims, the claimed objectives must be inherent in the prior art method, whether expressly disclosed or not.

In view of the currently amended claim 11 and the attached Declaration, Applicants submit that this rejection no longer applies. The attached Declaration disqualifies Koike as §102(a) art. Support for the amendment to claim 11 is found in paragraphs 6, 8, 24, 37 and Example I of the specification. Furukawa does not teach or even suggest the administration of vitamin K-II (menatetrenone) after a patient has received hepatocellular carcinoma treatment. Accordingly, Applicants submit that

currently amended claim 11 is in condition for allowance and respectfully request withdrawal of this rejection.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 1-9 and 11-15 under 35 U.S.C. §103(a) as being unpatentable over Furukawa or Koike in view of Wang *et al.* (Wang *et al.*, Hepatology, Vol. 22, pp. 876-882, September 1995) (hereinafter "Wang"). The Examiner has alleged that, if not inherently disclosed, a difference between the above and the claimed subject matter would lie in that none of the references disclose that the recurrence of hepatocellular carcinoma could be inhibited. The Examiner has further alleged that to the skilled artisan, the claimed subject matter would nevertheless have been obvious because Applicants acknowledge that the claimed compound menatetrenone was a known vitamin K compound and that Wang teaches that the vitamin K compounds inhibit the growth of hepatocellular carcinoma (HCC). The Examiner has stated that the skilled artisan would have been motivated to employ menatetrenone to inhibit the recurrence of HCC because of menatetrenone's known anti-HCC characteristics as taught by Wang and the desire to not have a patient who has suffered from hepatic cancer not to suffer from that cancer again. Applicants respectfully traverse this rejection. In view of cancelled claims 1-9 and 12-15, this rejection is moot with regard to those claims.

With regard to currently amended claim 11, Applicants submit that this rejection no longer applies. As discussed *supra*, the enclosed Declaration disqualifies Koike as §102(a) art. Wang does not cure the deficiencies of Furukawa. Wang does not teach or

suggest the administration of vitamin K-II to a patient after the patient has been treated for hepatocellular carcinoma. Accordingly, Applicants submit that claim 11 is in condition for allowance and respectfully request withdrawal of this rejection.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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